

### **REMARKS**

Claims 2, 4-7, 15, 16, 24, 25, 27, 28, 36-38, 40, 43, 44 and 60 are pending. Claim 26 has been canceled. Claim 60 was amended. The claim amendment and cancellation should not be construed to be an acquiescence to any of the claim rejections. Rather, the amendments to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to further prosecute claims drawn to canceled or deleted subject matter in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

### ***Request for Withdrawal of Premature Final Rejection***

The Applicants respectfully request withdrawal of the Final Rejection in the outstanding Office Action. The Applicants contend that the finality of the Office Action was inappropriate because the Examiner introduced a new grounds of rejection based on Mao *et al.*, Biodegradable Polyphosphoesters, Encyclopedia of Controlled Drug Delivery, 1999. The Examiner states that “due to a review of the teachings of the applied reference a rejection under 35 U.S.C. § 103(a) over Wen *et al.* in view of Mao *et al.* is cited” relying on the contention that Mao *et al.* discloses “biodegradable polyphosphoester particles...sized between 3 and 50  $\mu\text{m}$ .” However, the subject matter “microspheres having a mean diameter of less than about 250 microns” was already in claim 24. Hence, the rejection on the grounds of Wen *et al.* in view of Mao *et al.* could have been made in the prior Office Action; in other words, the rejection was not made on the basis of a claim amendment. In addition, Mao *et al.* was not listed on an Information Disclosure Statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p). The MPEP states “under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).” MPEP § 706.07(a). Accordingly, the Applicants request withdrawal of the Final Rejection.

**Response to Rejections under 35 U.S.C. § 103**

Claims 2-7, 24-28, 36-38, 40, 43, 44 and 60 were rejected under 35 U.S.C. § 103 as being unpatentable over Wen *et al.* in view of Mao *et al.* The Examiner contends that “there are no unusual and/or unexpected results which would rebut prima facie obviousness.” The Applicants respectfully traverse this rejection for at least the following reasons.

The data in Figure 26 illustrates that microspheres comprising a radiosensitizer and a biocompatible polymer having phosphorus-based linkages provide unexpectedly good tumor suppression in mice receiving radiation therapy. For example, at day 15 in Figure 26, mice receiving radiation therapy and microspheres of a biocompatible polymer having phosphorus-based linkages had tumors that had grown to approximately 250 mm<sup>3</sup> in volume, whereas mice receiving microspheres comprising a radiosensitizer and a biocompatible polymer having phosphorus-based linkages had tumors that shrunk to less than about 100 mm<sup>3</sup> in volume. The Applicants contend that one of ordinary skill in the art would not have reasonably expected that microspheres comprising a radiosensitizer and a biocompatible polymer having phosphorus-based linkages would cause a reduction in tumor volume of this magnitude in mice receiving radiation therapy.

In addition, the Applicants point out that there was no reasonable expectation of success that combining Wen *et al.* and Mao *et al.* would result in the claimed invention. The Applicants point out that Wen *et al.* did not test performance of the microspheres reported therein for treating tumors, nor did Wen *et al.* test how the microspheres reported therein would react to treatment with radiation. As described on page 1061 of Cecil’s Textbook of Medicine (previously of record), radiation reacts with molecular oxygen to form reactive species, such as superoxide, hydrogen peroxide or hydroxyl radicals. Wen *et al.* does not teach how the microspheres reported therein might behave in the presence of such reactive species. Accordingly, based merely on the teachings of Wen *et al.* and Mao *et al.*, one of ordinary skill in the art would not have reasonably expected that the microspheres claimed in the instant application would cause such a reduction in tumor volume in mice receiving radiation therapy. The Applicants respectfully remind the Examiner that “references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention,” and that “a determination under 35 U.S.C. 103 should rest on all the evidence and should not be influenced

by any earlier conclusion.” See MPEP § 2141 and 2144.08. In view of the foregoing, the Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103 based on *Wen et al.* in view of *Mao et al.*


### **FEES**

The Applicants believe they have provided for the required fees in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any additional required fee to our Deposit Account, **06-1448**.

### **CONCLUSION**

In view of the foregoing remarks, early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-832-1000.

Respectfully submitted,  
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